

Correlating CD4 count with mucocutaneous manifestations in HIV-positive patients: A prospective study

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Abstract

Background: Mucocutaneous findings may be the presenting symptoms in HIV-afflicted individuals. A multitude of mucocutaneous diseases also occurs during the course of the ailment, with some conditions being classed as disease defining. They include infectious diseases and noninfective inflammatory and neoplastic dermatoses. With progressive fall in CD4 count, there is a change in the types of mucocutaneous lesions encountered. **Aim:** This study aims to statistically correlate the CD4 counts with the mucocutaneous manifestations in 100 HIV-positive patients. **Materials and Methods:** A total of 100 cases of HIV-positive patients with skin and mucous membrane manifestations were selected serially. A complete history was taken, clinical examination was done, and the CD4 count was noted. Patients were divided into four groups (Groups I, II, III, IV) with different ranges of CD4 values, namely, <50, 50–200, 201–500, >500, respectively. **Results:** The distribution of study population in CD4 ranges showed that majority (47%) of the study population had CD4 count between 201 and 500, and 29% of the study group had CD4 count between 50 and 200 cells. Almost 21% of the patients had the count > 500 cells and 3% had cell count < 50. Majority of the infectious and non-infectious dermatoses were common in the CD4 count between 201–500 (Group III) and 50–200 (Group II). In the study groups, 52 cases (52%) were on antiretroviral therapy (ART), and the remaining 48 cases (48%) were not on ART at the time of diagnosis of mucocutaneous manifestations. Out of 48 ART-naïve cases, 23 patients were screened and newly diagnosed at the outpatient department (OPD) based on the mucocutaneous manifestations. Most of the patients with multiple mucocutaneous conditions were in the CD4 count <200, whereas single manifestation was seen predominantly in CD4 count >200. **Conclusion:** Statistically significant association with the CD4 count was seen in herpes zoster ophthalmicus, genital wart, genital herpes, vaginal discharge syndrome, scabies, pyoderma, dermatophytosis, Hansen's disease, herpetic gingivostomatitis, seborrhoeic dermatitis, lichen planus, and drug reactions. These dermatoses may indicate the worsening of immune status and the need for regular monitoring with periodical CD4 counting. Occurrence of dermatoses such as photosensitive eczema, drug reaction, lichen planus, Type I lepra reaction, and herpes zoster ophthalmicus in patients on ART may be due to IRIS. To avoid the more frequent occurrence of infectious dermatoses and to reduce the development of IRIS with ART, all HIV-positive cases may be started on ART at higher CD4 count. Screening for HIV infection is suggested whenever the following conditions are seen: persistent oral candidiasis, atypical manifestations of zoster, herpes zoster ophthalmicus, herpetic gingivostomatitis and MC in adults, exaggerated IBA, and extensive seborrhoeic dermatitis.

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Key words: CD4 count, HIV positive patients, immune reconstitution inflammatory syndrome, mucocutaneous manifestations, prognostic markers

INTRODUCTION

HIV-positive patients present with wide range of mucocutaneous signs and symptoms. These skin conditions may be influenced by the stage of the disease, immune status of the patient, and medication taken. Many mucocutaneous manifestations may help in diagnosing HIV-positive individuals. They may also serve as prognostic markers of the disease.

Aim of the study

This study aims to statistically correlate the CD4 counts with the mucocutaneous manifestations in 100 HIV-positive patients.

MATERIALS AND METHODS

A total of 100 cases of HIV-positive patients with skin and mucous membrane manifestations were selected serially. A complete history was taken, clinical examination was done, and the CD4 count was noted. Patients were divided into four groups (Groups I, II, III, IV) with different ranges of CD4 values, namely, <50, 50–200, 201–500, >500, respectively. The mucocutaneous manifestations in the four groups were noted and tabulated accordingly.

Ethical committee approval

This study was approved by our Institutional Ethics Committee.

Statistical analysis method

Statistical analysis was done using Chi-square test. $P < 0.05$ was considered as statistically significant.

OBSERVATION AND RESULTS

Among the 100 cases studied, 53 were male, and 47 were female. The majority of the patients were in the age group of 31–40 years [Figure 1]. Most of the study populations were farmers (35%) and laborers (35%) [Figure 2]. The distribution of study population in CD4 ranges showed that majority (47%) of the study population had CD4 count between 201 and 500 (Group III), and 29% of the study group had CD4 count between 50 and 200 cells (Group II). Almost 21% of the patients had the count >500 cells (Group IV) and 3% had cell count <50 (Group I) [Table 1].

Among the study population, 23 types of infectious and 18 noninfectious dermatoses were seen.

Out of 23 infectious dermatoses, 14 dermatoses occurred in 2 or more than 2 patients, namely, oral candidiasis (31 cases), genital herpes (8 cases), scabies (3 cases), dermatophytosis (8), herpetic gingivostomatitis (3), herpes zoster ophthalmicus (4), herpes zoster (6), cutaneous wart (3), genital wart (5), vaginal discharge syndrome (9), onychomycosis (2), Hansen’s disease (3), pyoderma (4), and molluscum contagiosum (MC) (2) [Table 2].

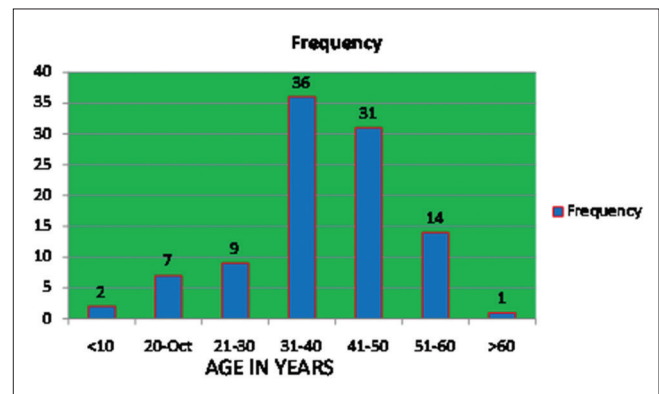


Figure 1: Age-wise distribution of the study population

Table 1: Distribution of the study population based on the CD4 count

Number of CD4 (cells/cmm)	Frequency	Percentage
<50 (Group I)	3	3
50-200 (Group II)	29	29
201-500 (Group III)	47	47
>500 (Group IV)	21	21
Total	100	100.0

Table 2: Prevalence of common infectious dermatoses in study population

Common infectious dermatoses	Number of cases (%)
Oral candidiasis	31 (35.1)
Vaginal discharge syndrome	9 (9.8)
Genital herpes	8 (8.7)
Dermatophytosis	8 (8.7)
Herpes zoster	6 (6.6)
Genital wart	5 (5.5)
Herpes zoster ophthalmicus	4 (4.3)
Pyoderma	4 (4.3)
Hansen’s disease	3 (3.2)
Cutaneous wart	3 (3.2)
Scabies	3 (3.2)
Herpetic gingivostomatitis	3 (3.2)
Onychomycosis	2 (2.1)
Molluscum contagiosum	2 (2.1)
Total	91 (100)

The majority of the infectious dermatoses were common in the CD4 count between 201–500 (Group III, 38 cases) and 50–200 (Group II, 30 cases), whereas vaginal discharge syndrome was more common among patients with CD4 count >500 (Group IV) [Table 3].

Among the infectious conditions, statistically significant association with the CD4 count was seen in herpes zoster ophthalmicus ($P < 0.004$), genital wart ($P < 0.033$), genital herpes ($P < 0.022$), vaginal discharge syndrome ($P < 0.012$), pyoderma ($P < 0.021$), dermatophytosis ($P < 0.046$), scabies ($P < 0.047$), Hansen’s disease ($P < 0.047$), and herpetic gingivostomatitis ($P < 0.047$) [Table 3].

Among the 18 noninfectious dermatoses, 6 dermatoses occurred in 2 or >2 cases. The common non-infectious dermatoses seen in our study were insect bite allergy (IBA, 21 cases), seborrhoeic dermatitis (10 cases), photosensitive eczema (4 cases), lichen planus (4 cases), vasculitis (2 cases), and drug reaction (2 cases) [Table 4].

Among the noninfectious dermatoses, most of the cases (26 cases) were seen in the CD4 range 201–500 (Group III), followed by 50–200 (Group II, 11 cases), and >500 (Group IV, 6 cases). None of the dermatoses were seen in CD4 <50 (Group I) [Table 5].

There was a statistically significant association with CD4 count seen in seborrhoeic dermatitis ($P < 0.041$), lichen planus ($P < 0.021$), and drug reaction ($P < 0.032$) [Table 5].

One case of squamous cell carcinoma of penis (CD4-114) and one case of palmoplantar psoriasis (CD4-359) were observed in this study.

In the study population, 55 patients (55%) had single dermatological condition, and 45 patients (45%)

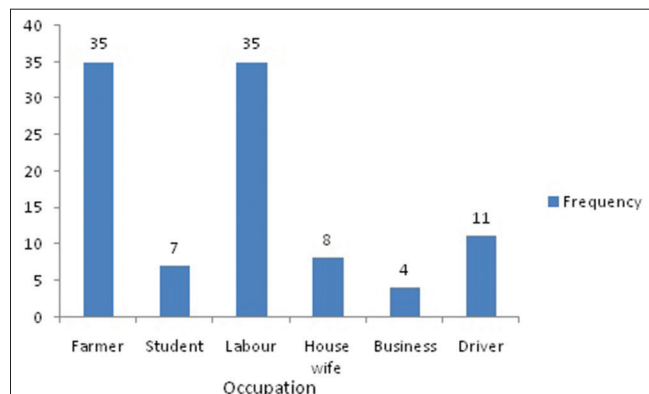


Figure 2: Occupation-wise distribution of the study population

had >1. Almost 26 patients with multiple conditions were in the CD4 range 50–200 (Group II). Single manifestation was seen predominantly in Group III (CD4, 201–500, 36 patients) and Group IV (CD4 >500, 16 patients) [Table 6].

In the study groups, 52 cases (52%) were on antiretroviral therapy (ART), and the remaining 48 cases (48%) were not on ART at the time of diagnosis of mucocutaneous manifestations. Out of 48 ART-naïve cases, 23 patients were screened and

Table 3: Association of infectious dermatoses with cd4 count

Clinical manifestations	CD4 count/cumm				Total	P
	<50	50-200	201-500	>500		
Oral candidiasis	1	12	13	5	31	0.0871
Genital herpes	0	4	4	0	8	0.022
Scabies	0	1	2	0	3	0.047
Dermatophytosis	1	3	2	2	8	0.046
Herpetic gingivostomatitis	0	1	2	0	3	0.047
Herpes zoster ophthalmicus	0	0	2	2	4	0.004
Cutaneous wart	0	1	1	1	3	0.638
Genital wart	0	1	3	1	5	0.033
Onychomycosis	0	0	1	1	2	0.731
Hansen’s disease	0	1	2	0	3	0.047
Pyoderma	0	4	0	0	4	0.021
Herpes zoster	0	3	3	0	6	0.531
Vaginal discharge syndrome	1	0	2	6	9	0.012
Molluscum contagiosum	0	0	1	1	2	0.376
Total	3	30	38	20	91	

Table 4: prevalence of common noninfectious dermatoses in study population

Common noninfectious dermatoses	Frequency (%)
Insect bite allergy	21 (48.8)
Seborrhoeic dermatitis	10 (23.2)
Photosensitive eczema	4 (9.3)
Drug reaction	2 (4.7)
Vasculitis	2 (4.7)
Lichen planus	4 (9.3)
Total	43 (100)

Table 5: Association of noninfectious dermatoses with CD4 count

Clinical manifestations	CD4 count/cumm				Total	P
	<50	50-200	201-500	>500		
Insect bite allergy	0	7	12	2	21	0.741
Seborrhoeic dermatitis	0	2	6	2	10	0.041
Photosensitive eczema	0	1	3	0	4	0.081
Drug reaction	0	0	2	0	2	0.032
Vasculitis	0	1	1	0	2	0.518
Lichen planus	0	0	2	2	4	0.021
Total	0	11	26	6	43	

newly diagnosed at the outpatient department (OPD) based on the mucocutaneous manifestations.

The majority of cases of dermatophytosis (7 cases), vaginal discharge syndrome (6 cases), and seborrhoeic dermatitis (6 cases) were seen in ART-naïve patients. All the cases of herpetic gingivo-stomatitis (three cases) and MC (two cases) were seen in ART naïve patients [Table 7].

All cases of pyoderma (four cases) were seen in patients on ART. Noninfectious dermatoses such as photosensitive eczema (four cases), drug reaction (two cases), and lichen planus (three cases) were seen in patients on ART [Table 8].

Among the infectious and noninfectious dermatoses, the distribution of oral candidiasis, genital herpes, herpes zoster, genital wart, IBA, and vasculitis were almost equal in both ART-naïve patients and on ART patient.

DISCUSSION

This study showed the distribution of mucocutaneous manifestations in different CD4 ranges and also showed the pattern of occurrence of dermatoses in patients on ART and in ART naïve patients.

The male-to-female ratio observed in our study was 1.2:1. The majority of the patients were in the age group of 31–40 years with a minimum age of 5 years and maximum age was 66 years. The mean age among the study population was 38.6 years.

Most of the study populations were farmers (35%) and laborers (35%). Since our hospital is in rural area, majority of the patients were farmers and laborers rather than drivers and migrants.

The distribution of study population in CD4 ranges showed that majority (47%) of the study population had CD4 count between 201 and 500 (Group III). ART-naïve patients in this Group III may progress to severe immunosuppression (CD4 <200). Hence, close monitoring with regular CD4 count estimation is necessary for these groups of patients.

The most common infectious dermatosis seen in this study was oral candidiasis (31 cases), followed by vaginal discharge syndrome (9 cases), genital herpes (8 cases), and dermatophytosis (8 cases).

The majority of the infectious dermatoses were commonly seen in CD4 count <500, whereas vaginal

Table 6: Distribution of study population based on CD4 count and the number of lesions

CD4 count	Number of lesions		Total number of patients	χ^2	P
	Single	Multiple			
<50 (Group I)	0	3	3	18.838	<0.0001
50-200 (Group II)	3	26	29		
201-500 (Group III)	36	11	47		
>500 (Group IV)	16	5	21		
Total	55	45	100		

Table 7: Distribution of Infectious dermatoses in antiretroviral therapy and preantiretroviral therapy patients

Infectious dermatoses	Pre-ART	ART	Total
Oral candidiasis	15	16	31
Genital herpes	4	4	8
Scabies	1	2	3
Dermatophytosis	7	1	8
Herpetic gingivostomatitis	3	-	3
Herpes zoster ophthalmicus	1	3	4
Cutaneous wart	1	2	3
Genital wart	2	3	5
Onychomycosis	1	1	2
Hansen's disease	1	2	3
Pyoderma	-	4	4
Herpes zoster	3	3	6
Vaginal discharge syndrome	6	3	9
Molluscum contagiosum	2	-	2
Total	47	44	91

ART=Antiretroviral therapy

Table 8: Distribution of noninfectious dermatoses in antiretroviral therapy and antiretroviral therapy-naïve cases

Noninfectious dermatoses	Pre-ART	ART
Insect bite allergy	10	11
Seborrhoeic dermatitis	6	4
Photosensitive eczema	-	4
Drug reaction	-	2
Vasculitis	1	1
Lichen planus	1	3
Total	18	25

ART=Antiretroviral therapy

discharge syndrome cases were more common among patients with CD4 count >500 (Group IV).

Oral candidiasis was the most common infectious dermatosis in this study seen in all CD4 ranges. This is in par with the previous study by Kore *et al.*^[1]

The high prevalence of sexually transmitted infections (STI) was noted in our study (24%). These data were similar to the previous study by Kore *et al.*^[1] Vaginal discharge syndrome was the

most common STI observed in this study, followed by genital herpes and genital wart [Figure 3].

Among the infectious conditions, statistically significant association with the CD4 count was seen in herpes zoster ophthalmicus ($P < 0.004$), genital wart ($P < 0.033$), genital herpes ($P < 0.022$), vaginal discharge syndrome ($P < 0.012$), pyoderma ($P < 0.021$), dermatophytosis ($P < 0.046$), scabies ($P < 0.047$), Hansen's disease ($P < 0.047$), and herpetic gingivostomatitis ($P < 0.047$).

Genital herpes and pyoderma cases were seen mainly in Group II (CD4, 50–200) may be considered as markers of severe immunosuppression.

Herpetic gingivostomatitis patients had severe mucosal erosions and dysphagia due to pharyngeal involvement [Figure 4]. Genital herpes cases were more common than oral herpetic infections which were similar to the study conducted by Sarna *et al.*^[2]

Among the three scabies cases, two cases were crusted scabies. Crusted scabies in sexually active adults in the absence of neurological or psychiatric conditions could be considered as a marker of HIV.

All the three cases of Hansen's disease were in borderline tuberculoid spectrum, of these two cases on ART were in Type I lepra reaction due to immune reconstitution inflammatory syndrome (IRIS).^[3]

Exaggerated IBA (21 cases) was the most common noninfectious dermatosis observed in this study, followed by seborrhoeic dermatitis (10 cases). A similar pattern was noted by Halder *et al.* in their study.^[4]

Among the noninfectious dermatoses, most of the cases were seen in the CD4 range 201–500 (Group III, 26 cases) and none of the dermatoses were seen in CD4 <50 (Group I) which indicates the important role of T-lymphocytes in noninfectious dermatoses observed in this study.

There was a statistically significant association with CD4 count seen in seborrhoeic dermatitis ($P < 0.041$), lichen planus ($P < 0.021$), and drug reaction ($P < 0.032$).

One case of squamous cell carcinoma of penis (CD4-114) and one case of palmoplantar psoriasis (CD4-359) were observed in this study. Low prevalence of malignancies was observed in this study which was similar to the previous studies by Wiwanitkit and Chawhan.^[5,6]

As majority of seborrhoeic dermatitis, lichen planus, photosensitive eczema, and drug reaction cases were seen in Group III, these cases may be considered as forerunner of severe immunosuppression and indicate the need for monitoring HIV disease progression.

Generalized lichen planus with oral involvement was seen in all the three out of four cases of lichen planus.

Drug reactions observed in our study were not due to ART drugs. Hence, detailed history of other drugs intake is necessary in all ART patients with drug reactions. HIV infected patients may have recurrent cutaneous reactions due to ant tuberculosis drugs, other antibiotics, and nonsteroidal anti-inflammatory drugs.^[7]

Vasculitis (two cases) patients had only tender erythematous plaques in both palms and soles without any other associated infections [Figure 5].

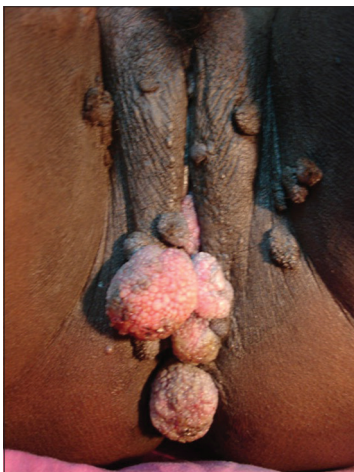


Figure 3: Giant condyloma (CD4-235)



Figure 4: Herpetic gingivostomatitis in an adult male (CD4-230)

Vascular inflammation in HIV occurs as a result of infections, drugs, or by nonspecific mechanisms.^[8]

Most of the patients with multiple mucocutaneous conditions were in the CD4 count <200, whereas single manifestation was seen predominantly in CD4 count >200 (Group III and Group IV).

Multiple diagnoses were common among patients with lesser CD4 count, and single was predominantly seen in higher CD4 range, and this difference was found to be statistically significant ($P < 0.0001$).

In the study population of 48 ART-naïve cases, 23 patients were screened and newly diagnosed at the OPD based on the mucocutaneous manifestations. Exaggerated IBA was the most common dermatosis seen in newly diagnosed cases [Figure 6]. Exaggerated IBA in HIV-positive patients occur as a result of reversal of CD4:CD8 ratio, shift from Th1 to Th2 response and recall the reaction to arthropod bites.^[9]

Among the infectious and noninfectious dermatoses, the distribution of oral candidiasis, genital herpes, herpes zoster, genital wart, IBA, and vasculitis were almost equal in both ART-naïve patients and in patients on ART. From these observations, we found that the variation in CD4 count due to ART does not influence the occurrence of these dermatoses.

The majority of cases of dermatophytosis (seven cases), vaginal discharge syndrome (six cases), and seborrhoeic dermatitis (six cases) were seen in ART-naïve patients, in our study.

All the cases of herpetic gingivostomatitis (three cases) and MC (two cases) were seen in ART-naïve patients. This observation indicated that ART may be beneficial in preventing the occurrence of the infectious dermatoses such as dermatophytosis, vaginal discharge syndrome, herpetic gingivostomatitis, and MC.

MC lesions were seen on the face in these cases [Figure 7]. Hence in adults, MC lesions on the face and severe herpetic gingivostomatitis may be considered as markers of HIV and screening may be done for these cases.

All cases of pyoderma (four cases) and Hansen's disease cases with Type I lepra reaction, (two cases) and three cases of herpes zoster ophthalmicus [Figure 8] were seen in patients on ART.



Figure 5: Vasculitis with erythematous plaques in palm (CD4-144)



Figure 6: Exaggerated insect bite allergy in exposed sites (CD4-425)



Figure 7: Molluscum contagiosum on the face of a young female (CD4-361)



Figure 8: Herpes zoster ophthalmicus in a boy (CD4-607)

Noninfectious dermatoses such as photosensitive eczema (four cases), drug reaction (two cases), and lichen planus (three cases) were seen in patients on ART.

The occurrence of most of the dermatoses such as photosensitive eczema, drug reaction, lichen planus, herpes zoster ophthalmicus, and Type I lepra reaction in ART patients may be due to IRIS.^[10] Among these conditions, the noninfectious dermatoses have occurred in an exaggerated manner and required systemic steroid for longer duration than their HIV-negative counterparts, which also indicates that they should be watched regularly for the side effects of steroids.

CONCLUSION

The results of our study showed that 47/100 cases were seen in Group III (CD4, 201–500).

Statistically significant association with the CD4 count was seen in herpes zoster ophthalmicus, genital wart, genital herpes, vaginal discharge syndrome, scabies, pyoderma, dermatophytosis, Hansen's disease, herpetic gingivostomatitis, seborrhoeic dermatitis, lichen planus, and drug reactions. These dermatoses may indicate the worsening of immune status and the need for regular monitoring with periodical CD4 counting.

Most of the infectious dermatoses were seen in CD4 count <500 except vaginal discharge syndrome which was more commonly seen in CD4 count >500.

Infectious diseases seen in advanced immunosuppression such as atypical mycobacterial infections, disseminated systemic fungal infection, and chronic herpes simplex virus infection were not seen in our study.

Viral STIs were more commonly seen than bacterial STI as per the current trend.

None of the eczematous and noninfectious dermatoses were seen in CD4 count <50 which indicates that these dermatoses may not occur in advanced in AIDS due decreased cell-mediated immune response. Clinically, the development of more number of infectious dermatoses and decreasing frequency of noninfectious dermatoses indicate the deterioration of immune status.

Malignancies seen in advanced stage were not seen in our study except one case of squamous cell carcinoma of penis.

Although oral candidiasis and IBA were the most common manifestations seen, they could not be correlated statistically with the CD4 counts, which may be attributed to the sample size.

Exaggerated IBA was the most common manifestation seen in newly detected cases.

The occurrence of most of the dermatoses such as photosensitive eczema, drug reaction, lichen planus, Type I lepra reaction, and herpes zoster ophthalmicus in patients on ART may be due to IRIS. Noninfectious IRIS needs to be administered steroid for longer duration.

To avoid the more frequent occurrence of infectious dermatoses and to reduce the development of IRIS with ART, all HIV-positive cases may be started on ART at higher CD4 count.

Most of the findings of our study correlated well with the previous studies with reference to both infectious and noninfectious diseases.

Screening for HIV infection is suggested whenever the following conditions are seen: persistent oral candidiasis, atypical manifestations of zoster, herpes zoster ophthalmicus, herpetic gingivostomatitis and MC in adults, exaggerated IBA, and extensive seborrhoeic dermatitis.

We conclude that mucocutaneous manifestations may serve as diagnostic and prognostic markers of HIV in clinical practice. These findings are good clinical indicators to predict immune status and also to some extent predict the stage of the disease where facilities for CD4 count are not available and to initiate treatment in resource-poor places.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that

their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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